

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 11

REMARKS

Claims 1-14, 17-32, 34-43, 60 and 61 are currently pending in the application. Claims 15, 16, 33 and 44-59 are canceled. Claims 1-14 and 17-24 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

I. Finality of the Office Action

The Office Action was made final on the basis that "Applicants' amendment necessitated the new grounds of rejection presented in this Office Action". Applicants respectfully traverse the finality of the Office Action.

Applicants submit that the finality of the present Office Action is premature because it introduces new grounds of rejection that were not necessitated by Applicants' amendments. Basis for Applicants' request for removal of the finality of the Office Action is set forth below.

II. Claim Rejections – 35 U.S.C. § 112, First Paragraph

Claims 1-14, 16-43 and 60-61 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

The Office Action states that the recitation "attached directly" in the amended independent claims 1 and 24 is not supported by any disclosure in the specification. The Office Action also states that the "claimed 'attached directly' encompasses numerous and various attachments" and that the "claimed attachment encompasses a very large genus of attachments". The Office Action states, based on the above presumption, that the amendment introduces new matter since the specification "does not teach the broadly claimed attachment". Applicants respectfully traverse the rejection, on the following grounds.

Section 706.07(a) Final Rejection, When Proper on Second Action [MPEP] states that "Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 12

applicant's amendment of the claims nor based on information submitted in an information disclosure statement" (emphasis added).

Applicants submit that the term "directly attached" in the amended independent claims 1 and 24 (from which all other claims depend) describes the mode of attachment of the nanotubes to the substrate surface. The Office Action, however, acknowledges that the specification "teaches the carbon nanotube grown on a substrate (e.g. page 12, lines 21-23)" which is an embodiment that necessarily requires "direct attachment" of the carbon nanotubes to the substrate. Figures 1, 3, 4, 5 and 7-9 in the specification show examples of carbon nanotubes grown on the substrate surface wherein they are directly attached to the substrate. In an earlier Office Action dated November 10, 2003, the Examiner rejected independent claim 1 under §112, second paragraph, as being indefinite for the recitation "said proximal ends *being* attached to substrate" "because it is unclear whether the proximal ends are attached to the substrate or whether the recitation is a method step for attaching the proximal ends at some time in the future". That Office Action further stated that "[i]t is suggested that the claim be amended to clarify e.g. delete '*being*'".

Applicants submit that no reference was made in that earlier Office Action that the term "attached" in claim 1 was (i) not supported by the disclosure in the specification, and (ii) it encompasses a very large genus of attachments and does not teach the broadly claimed attachment. No reference was made in that Office Action as to the specification not teaching the claimed attachment. On the other hand, the § 112, second paragraph indefiniteness rejection of claim 1 was directed only toward the term "*being*" in claim 1, and applicants amended claim 1 to recite "attached directly" and deleted the term "*being*" in accordance with the Examiner's suggestion to cure the indefiniteness. Support for the amendment is found in the specification which the Final Office Action affirms.

The Office Action states that "the instantly claimed "attached directly" encompasses numerous and various attachments e.g. attachment of pre-made nanotube onto a substrate via a linker, via a functional group, via covalent bond, via hydrogen bond, via hydrophilic/hydrophobic interaction and etc". The Office Action also states that, "[a]s such, the

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 13

instantly claimed attachment encompasses a very large genus of attachments" and that "[i]n contrast, the specification teaches a single means of attachment i.e. growth of the nanotube". The Office Action concludes that "[b]ecause the specification does not teach the broadly claimed attachment, the amendment introduces new matter". Applicants submit that the recitation "attached directly" in amended claims 1 and 24 cannot be, by definition, broader than the term "attached" as recited in claim 1 prior to amendment, since that term would also necessarily encompass the "numerous and various attachments" that is stated to be encompassed by the term "attached directly". Applicants, submit therefore, that the amendment of the term "attached" to "attached directly", merely clarifies the mode of attachment to be "without a linker" (see response to Office Action dated November 10, 2003). Applicants submit therefore, that the term "attached directly" in the amended claims 1 and 24, does not introduce new matter.

The above explanation was not presented at the time of amending claims 1 and 24 because the applicant did not fully understand or appreciate the nature of the Examiner's position with regard to the amendment until applicant was advised in detail of that position by the final rejection. Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

III. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claim 16 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action stated that claim 16 "is indefinite for the recitation 'at least two nanotube tubules' because the recitation lacks proper antecedent basis in the 'at least one' of claim 1". Claim 16 has been canceled. Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 14

IV. Rejection of Claims 1, 3-5, 7-8, 11-14 and 17-23 Under 35 U.S.C. § 103(a)

Claims 1, 3-5, 7-8, 11-14 and 17-23 are rejected under 35 U.S.C. §103(a) as being unpatentable over Colbert (WO 98/05920) in view of Lieber. (U.S. Patent No. 6,159,742).

The Office Action states that Colbert. "teach the nanotube comprises a metallic material but they do not specifically teach the metallic material is at the distal end wherein the biological compound is attached to the metallic material". The Office Action also states that "however, carbon nanotubes having metallic material at distal ends for attachment of biomolecules was well known in the art at the time the claimed invention was made as taught by Lieber.". The Office Action concludes that "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the carbon nanotube of Colbert. by attaching the biomolecule to metallic material at the distal end of the nanotube for the expected benefit of measuring binding force between single protein-ligand pairs as taught by Lieber.".

The Office Action states Colbert teaches a carbon nanotube array and an electrically conductive biological compound attached to the nanotube, but that Colbert does not specifically teach the metallic material is at the distal end wherein the biological compound is attached to the metallic material. The Office Action also states that carbon nanotubes having metallic material at distal ends for attachment of biomolecules was "well known in the art" citing Leiber (Fig. 1), and that Leiber further teaches binding of a biomolecules to the nanotubes to measure binding forces between single protein-ligand pairs. Applicants respectfully traverse this rejection.

The instant invention discloses a carbon nanotube array wherein the nanotube tubules comprise a metallic material at the distal end, and attached to an electrically conductive biological compound that provides electrical connectivity between the carbon nanotube tubules

Claim 1 has been amended to recite that the array comprises a pair of electrically conducting carbon nanotube tubules. Support for the amendment is found throughout the specification, for example at page 4, line 21, page 5, lines 11 through 13, and original claim 24. Claim 1 has also been amended to recite that the biological compound provides electrical connectivity between the pair of carbon nanotube tubules. Support for the amendment is

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 15

found throughout the specification, for example, at page 4, lines 19 through 22 and original claim 16.

Neither Colbert. nor Lieber alone or in combination, teach or suggest **providing electrical connectivity between a pair of nanotube tubules with an electrically conductive biological compound**. Since neither Colbert nor Lieber, teach or suggest every element of claim 1 in the invention, they do not render claim 1 or any of its dependent claims obvious. Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

V. Rejection of Claims 2 and 16 Under 35 U.S.C. § 103(a)

Claims 2 and 16 are rejected under 35 U.S.C. §103(a) as being unpatentable over Colbert in view of Lieber as applied to Claim 1 above and further in view of Saraf (U.S. Patent No. 6,656,693) or Mirkin (U.S. Patent No. 6,506,564) or Connolly (U.S. Patent No. 6,399,303).

The Office Action states that "*Colbert and Lieber disclose a carbon nanotube array device*" but "*do not teach a pair of nanotubes bridged by the electrically conductive compound.*" The Office Action also states that "however bridging electrically conductive biological compounds was well known in the art at the time the claimed invention was made as taught by each of Saraf, Mirkin and Connolly". The Office Action states that "Saraf teach a device comprising a substrate having pairs of electrodes coated with metallic material positioned proximally on the substrate wherein the distal ends of the electrodes are bridged by electrically conductive DNA". The Office Action states that "Mirkin also teach a device comprising a substrate having pairs of electrodes positioned proximally and bridged by electrically conductive DNA whereby target DNA are detected". The Office Action states that "Connolly teaches a device comprising a substrate having pairs of electrodes positioned proximally and bridged by electrically conductive DNA". The Office Action concludes that "bridging of biological compounds between arrayed structures to establish electrical contact between the structures was well known in the art at the time the claimed invention was made" and that "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrayed carbon nanotubes of Colbert and Lieber by bridging biological compounds between

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 16

them as taught by Saraf, Mirkin and Connolly . . . based the teaching of Saraf wherein the device overcomes problems associated with photolithographic techniques and/or based on the extremely sensitive target detection taught by Connolly and/or based on the dramatic increase in conductivity whereby thousands of complementary DNA targets can be detected simultaneously as taught by Mirkin". Applicants respectfully traverse the rejection.

Independent claim 1 has been amended to recite that the array comprises **a pair of carbon nanotube tubules** and that the biological compound **provides electrical connectivity between the pair of carbon nanotube tubules**. Neither Colbert nor Lieber, alone or in combination, teach or suggest a biological compound **providing electrical connectivity between the pair of carbon nanotube tubules**. The references of Saraf, Mirkin or Connolly alone or in combination do not remedy this deficiency, since none of the references teach the use of a biological compound to **provide electrical connectivity between the pair of carbon nanotube tubules in a carbon nanotube array**.

Connolly teaches sets of two oligonucleotide probes that requires the leads (referred to as "*pairs of electrodes*" in the office action) having end located close together, **but not contacting one another so as to present effective flow of current between leads without the presence of a target nucleic acid molecule to bridge the two leads** (Connolly Col. 2, lines 46-50). The instant invention requires **electrical connectivity between the carbon nanotube tubules via bridging of the tubules by an electrically conductive biological molecule so as to provide electrical connectivity between the carbon nanotubules in the absence of a target nucleic acid**. In fact, Connolly teaches away from the oligonucleotide probes providing electrical contact by stating that "the oligonucleotide probes are positioned such that the probes **cannot come into contact with one another**" (Column 1, lines 43 through 44).

Mirkin teaches bridging a pair of gold electrodes by a nanoparticle assembly that involves modification of the glass surface between them with oligonucleosides (Col. 92, lines 31-34) a plurality of gold nanoparticles that contain attached oligonucleosides. A mixture of target DNA and gold nanoparticles modified with oligonucleotides is added to the electrode assembly, following by treatment with a silver staining solution. (see Figure 41 at sheet 47 and

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 17

Example 22 at Col. 92, lines 41-49). Mirkin states that "only complementary target DNA strands form nanoparticle assemblies between the two electrodes of the device and that the circuit is completed by nanoparticle hybridization and subsequent silver staining. (Col.92, lines 59-63). Mirkin does not teach or suggest bridging carbon nanotubes with an electrically conductive compound **without a nanoparticle assembly and in the absence of target DNA** so as to provide electrical connectivity between the tubules, as claimed in the instant invention.

Saraf teaches bridging of a pair of electrodes with a biological compound to establish an electrical contact by using the "self-organizational nature of some biological molecules" (Col. 2, lines 63-64. Although Saraf states that such bridging overcomes problems associated with photolithographic techniques, the advantage is specifically directed to the bridging step, and not to the fabrication of the electrodes themselves. In fact, Saraf states that the electrodes themselves are formed on a substrate surface "according to common photolithographic techniques." (Col. 3 lines 20-22). Saraf does not disclose or suggest the fabrication of a carbon nanotube array and their modification with a metallic material at the tubule terminal ends to enable them to function as electrodes that are bridged with an electrically conductive biologic compound to provide electrical connectivity between the tubules, as claimed in the present invention.

None of the references cited provide any motivation to combine the teachings of Colbert and Lieber with the teachings of Saraf, Mirkin or Connolly to arrive at applicants claimed invention. Applicants believe their invention is being used as a blueprint for hindsight assembly of the cited references. Thus it is only through knowledge of the Applicants' specification describing the instant invention that a person skilled in the art would combine the nanotube tubules array taught in Colbert, the metallic coating of terminal ends of the carbon nanotube tubules taught in Lieber, bridging of conventional electrodes or electrode leads with biological compounds taught in Connolly, Mirkin and Saraf to arrive at Applicants' claimed invention.

"Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 18

patentability -- the essence of hindsight." *In re Dembiczak* (50 USPQ2d 1614 (Fed. Cir. 1999)).

As stated hereinabove, none of the references cited in the Office Action provide any motivation to combine the teachings of Colbert and Lieber with the teachings of Saraf, Mirkin or Connolly to arrive at applicants claimed invention. Without such motivation the references do not render independent claim 1 obvious. Dependent claims 2 and 16 depend from independent claim 1. Since Colbert, Lieber, Mirkin and Connolly alone or in combination do not render independent claim 1 obvious, those references do not render any dependent claims obvious as well. Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

VI. Rejection of Claims 24-27, 29-30, 32-39, 41-43, 60 and 61 Under 35 U.S.C. § 103(a)

Claims 24-27, 29-30, 32-39, 41-43, 60 and 61 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Colbert in view of Lieber and further in view of Saraf, Mirkin or Connolly.

The Office Action states that "Colbert and Lieber disclose a carbon nanotube array device" but "do not teach a pair of nanotubes bridged by the electrically conductive compound". The Office Action also states that "however bridging electrically conductive biological compounds was well known in the art at the time the claimed invention was made as taught by each of Saraf, Mirkin and Connolly". The Office Action states that "Saraf teach a device comprising a substrate having pairs of electrodes coated with metallic material positioned proximally on the substrate wherein the distal ends of the electrodes are bridged by electrically conductive DNA". The Office Action states that "Mirkin also teach a device comprising a substrate having pairs of electrodes positioned proximally and bridged by electrically conductive DNA whereby target DNA are detected". The Office Action states that "Connolly teaches a device comprising a substrate having pairs of electrodes positioned proximally and bridged by electrically conductive DNA". The Office Action concludes that "bridging of biological compounds between arrayed structures to establish electrical contact between the structures was well known in the art at the time the claimed invention was made" and that "it would have been

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 19

obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrayed carbon nanotubes of Colbert and Lieber by bridging biological compounds between them as taught by Saraf, Mirkin and Connolly . . . based the teaching of Saraf wherein the device overcomes problems associated with photolithographic techniques and/or based on the extremely sensitive target detection taught by Connolly and/or based on the dramatic increase in conductivity whereby thousands of complementary DNA targets can be detected simultaneously as taught by Mirkin". Applicants respectfully traverse the rejection.

Independent claim 24 is drawn to a molecular sensor device comprising a carbon nanotube electrode array comprising at least one pair of nanotube tubules and a biological compound that provides an electrical connectivity between the pair of nanotube tubules. Neither Colbert nor Lieber, alone or in combination, teach or suggest a biological compound providing an electrical connectivity between the pair of nanotube tubules. Saraf, Mirkin and Connolly alone or in combination, do not remedy this deficiency for the same reasons described in Section V of this reply.

None of these cited references, therefore, would provide any motivation for a person skilled in the art to combine the teachings of Colbert and Lieber, and then combine those teachings with the teachings of Saraf, Mirkin or Connolly to arrive at Applicants instant invention. Applicants believe the only way a person of ordinary skill would arrive at the instant invention is by using the instant invention as a blueprint for hindsight assembly of the cited references.

As stated hereinabove, none of the references provide any motivation to combine the teachings of Colbert and Lieber with the teachings of Saraf, Mirkin or Connolly to arrive at applicants claimed invention. Without motivation, the references do not render independent claim 24 obvious. Dependent claims 25-27, 29-30, 32-39, 41-43, 60 and 61 depend from independent claim 24. Since Colbert, Lieber, Saraf, Mirkin and Connolly alone or in combination do not render independent claim 24 obvious, those references do not render any dependent claims obvious as well. Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 20

VII. Rejection of Claim 6 Under 35 U.S.C. § 103(a)

Claim 6 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Colbert in view of Deguchi (U.S. Patent No. 6,400,091).

The Office Action states that "Colbert discloses a carbon nanotube array device comprising at least one nanotube with a proximal end and a distal end, said proximal end attached to a substrate and said tubule further comprising a metallic material wherein the metallic material is selected from one of several metals e.g. nickel, platinum or cobalt but they do not teach the metallic material is gold". The Office Action also states that "however, it was well known in the art at the time the claimed invention was made that carbon nanotube preferably contained gold as taught by Deguchi". The Office Action concludes that "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the nanotubes of Colbert by incorporating gold as taught by Deguchi". Applicants respectfully traverse the rejection.

Independent claim 1 has been amended to recite that the array comprises **a pair of nanotube tubules** and that the biological compound **provides electrical connectivity between the pair of nanotube tubules**. Colbert does not teach or suggest a biological compound that **provides electrical connectivity between the pair of nanotube tubules**. Deguchi does not remedy this deficiency. Deguchi does not teach or suggest a biological compound that **provides electrical connectivity between the pair of nanotube tubules**. Since neither Colbert nor Deguchi alone or in combination, teach or suggest a biological compound that **provides electrical connectivity between the pair of nanotube tubules**, the references do not teach or suggest every element of Applicants' claimed invention, therefore, they do not render independent claim 1 obvious. Dependent claim 6 depends from independent claim 1. Since Colbert, Lieber, Mirkin and Connolly alone or in combination do not render independent claim 1 obvious, those references do not render any dependent claims obvious as well. Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 21

VIII. Rejection of Claim 9, 10, 23, 31, 32 and 40 Under 35 U.S.C. § 103(a)

Claims 9, 10, 23, 31, 32 and 40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Colbert in view of Massey (U.S. Patent No. 5,866,434).

Regarding Claims 9, 10, 31 and 32, the Office Action states that "Colbert disclose a carbon nanotube array device comprising at least one nanotube with a proximal end and a distal end, said proximal end attached to a substrate and said tubule further comprising a metallic material but they do not teach the device wherein the metallic material is particulate". The Office Action also states that "however, Massey teach a similar device comprising at least one nanotube comprising metallic material at a terminal end wherein the metallic material is a magnetic bead". The Office Action concludes that "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the nanotubes of Colbert by providing a magnetic bead at a terminal end".

Regarding Claim 23 and 40, the Office Action states that "Colbert teach the device wherein the biological compound is DNA but they are silent regarding the DNA being single-stranded. The Office Action also states that "however, Massey teach the similar device wherein the biological compound is single-stranded DNA". The Office Action concludes that "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the single-stranded DNA of Massey to the DNA taught by Colbert". Applicants respectfully traverse the rejection.

Both independent claim 1 as amended and independent claim 24 recite that the array comprises a pair of nanotube tubules and that the biological compound provides electrical connectivity between the pair of nanotube tubules. Massey does not remedy this deficiency. Massey does not teach or suggest a biological compound providing electrical connectivity between the pair of nanotube tubules. Since neither Colbert nor Massey alone or in combination, teach or suggest a biological compound providing electrical connectivity between the pair of nanotube tubules, the references do not teach or suggest every element of

Attorney Docket No.: 2846/1032
Serial No.: 10/042,911
Page 22


Applicants' claimed invention, therefore, they do not render independent claim 1 or independent claim 24 obvious.

Claims 9, 10 and 23 depend from independent claim 1 and claims 31, 32 and 40 depend from independent claim 24. Since neither Colbert nor Massey render either independent claims 1 or 24 obvious, those references do not render any dependent claims obvious as well. Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Applicants submit that in view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed, and believe that the application has been placed in a condition for allowance. Applicants respectfully request the withdrawal of rejections over the claims of the present invention.

Respectfully submitted,

Date: August 24, 2004



Name: Sundar Subramanyam
Registration No.: 53,651
Customer No.: 29933
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel.: (617) 239-0100